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An Expedient Synthesis of Trisubstituted Allenes

Jack E. Baldwin*, Robert M. Adlington, Nicholas P. Crouch, Ryan L. Hill and Thomas G. Laffey

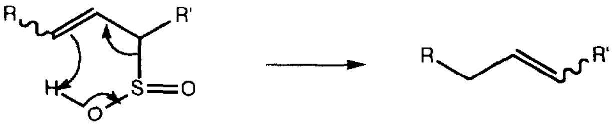
The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford, UK OX1 3QY

Abstract: *Di-α-alkylated-α-(β-keto sulfone) alkynes provide a facile entry to trisubstituted allenes upon treatment with aluminium amalgam.*

Allenes and higher cumulenes occur in several biologically active compounds , neocarzinostatin[1] being a recent example, and the well documented utility of allenes as synthetic intermediates has generated considerable interest in the development of improved routes to this functionality[2].

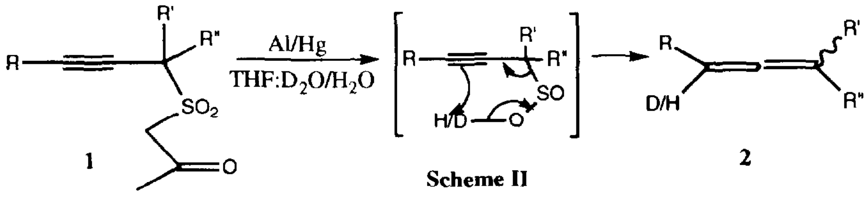
Recent investigations into novel methodology for C-C coupling of terminal alkenes necessitated the reduction of allyl β-keto sulfones. The sulfinic acids so formed are known to undergo retro-ene reactions with expulsion of sulfur dioxide to give alkenes (Scheme I)[3].

We report herein that exploitation of this retro-ene reaction with alkynyl sulfinic acids (generated by aluminium amalgam reduction of alkynyl β-keto sulfones) provides a simple high yielding and versatile method for the synthesis of trisubstituted allenes. (Scheme II).



Scheme I

In a typical example, Al/Hg mediated reduction of the alkynyl sulfones (1) in 10% aqueous THF at room temperature gave allenes (2) in 74% to 95% yield after 30 minutes. When the reaction was carried out in the presence of deuterium oxide, deuterium was regiospecifically incorporated into the product, providing further evidence for the intermediacy of a sulfinic acid.

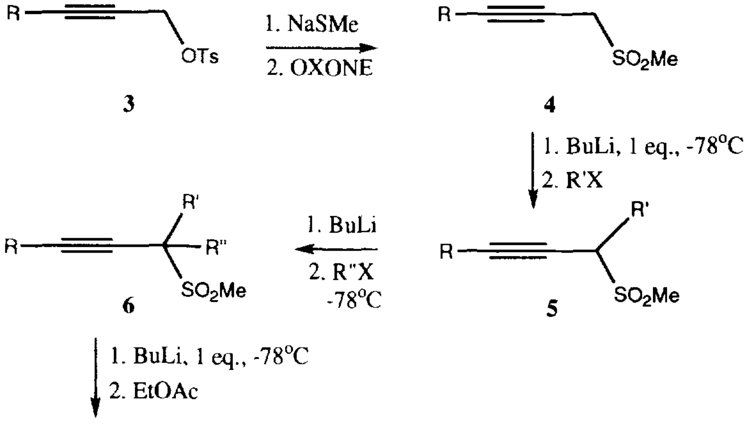


Scheme II

The requisite alkynyl β-keto-sulfones were prepared as depicted in Scheme III[4].

Attempts to prepare methyl sulfone, (4), by direct displacement of the corresponding tosylates with sodium methanesulfinate under a variety of conditions gave complex mixtures of products. However, tosylate displacement with sodium methanethiolate followed by oxidation with OXONE®[5] gave the methyl sulfone in 80% yield.

Deprotonation of the alkynyl sulfone in THF followed by an inverse quench with the appropriate alkyl halide gave 75-85%[6] of the α-alkylated product (5), along with less than 7% of di–α-alkylated material. Subsequent treatment of the mono-alkylated sulfone with nBuLi followed by quenching with various electrophiles resulted in satisfactory yields (80% - 92%)[7] of di-α-alkylated sulfones (6). Acylation of the α'-anion of the di-alkylated methyl sulfones (6) with ethyl acetate proceeded in satisfactory yield (60%-75%)[8] to give the desired alkynyl β-keto sulfones (1).



Scheme III

To illustrate the generality of this method for the preparation of allenes, a variety of alkynyl β-keto-sulfones were prepared[9] and subjected to reduction and concomitant rearrangement. The results are summarised in Table I and demonstrate that the aluminium amalgam mediated reduction of alkynyl-β-keto sulfones provides a simple, high yielding and versatile route to trisubstituted allenes[10].

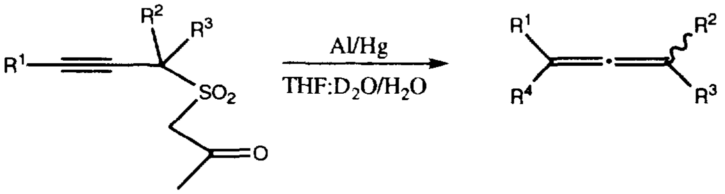


Table I

Entry	R^1	R^2	R^3	R^4	Solvent	Product yield‡
1.	Me	$(CH_3)_2C=CHCH_2$	$(CH_3)_2C=CHCH_2$	H	THF:H_2O	91%
2.	Me	$PhCH_2$	$PhCH_2$	H	THF:H_2O	85%
3.	Me	$PhCH_2$	nC_4H_9	H	THF:H_2O	86%
4.	Me	$(CH_3)_2C=CHCH_2$	$(CH_3)_2C=CHCH_2$	D	THF:D_2O	82%
5.	Me	$PhCH_2$	$PhCH_2$	D	THF:D_2O	86%
6.	Me	$PhCH_2$	$(CH_3)_2C=CHCH_2$	H	THF:H_2O	95%
7.	Et	$CH_3(CH_2)_4$	$CH_3(CH_2)_3$	H	THF:H_2O	74%
8.	Et	$PhCH_2$	$PhCH_2$	H	THF:H_2O	84%
9.	Pent	$(CH_3)_2C=CHCH_2$	$CH_3(CH_2)_3$	H	THF:H_2O	80%
10.	Bu	$PhCH_2$	$CH_3(CH_2)_4$	H	THF:H_2O	92%
11.	Pent	$CH_3(CH_2)_4$	$CH_3(CH_2)_3$	H	THF:H_2O	83%

‡ After chromatography

In summary, di-α-alkylated-α-(β-keto sulfone)-alkynes are readily prepared and efficiently transformed to tri-substituted allenes upon treatment with aluminium amalgam.

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4. All new compounds were characterised by combustion analysis and/or spectral data (IR, ^{1}H NMR, ^{13}C NMR and m/z).

5. OXONE®, monopersulfate compound (potassium peroxymonosulfate), $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Aldrich catalogue number 22,803-6; CAS number 37222-66-5)

6. For cases 7 and 11 the yield was approximately 60 %.

7. When using butyl and pentyl halides, the yields dropped to approximately 65 - 77 %.

8. As determined by ^{1}H NMR (200 MHz).

9. Routinely, the alkynyl-β-ketosulfones (1) were not purified from their precursors (6) (Scheme III) due to similar chromatographic properties. The yields in Table I were calculated taking into account the fact that only component (1) is transformed by the aluminium amalgam.

10. It is noteworthy that all the allenes were stable to chromatography on silica gel and elution with a hydrocarbon solvent enabled facile removal of traces of unreacted starting material.

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